

THE INFLUENCE OF
INTERNAL HEMORRHAGE ON CHEMICAL
CHANGES IN THE ORGANISM, WITH
PARTICULAR REFERENCE TO
PROTEIN CATABOLISM.

— BY —

FRED. S. WEINGARTEN, B.S., M.D.,

In collaboration with BURRILL B. CROHN, M.D.

DISSERTATION

Submitted in partial fulfilment of the requirements for the Degree of
Doctor of Philosophy, in the Faculty of Pure Science,
Columbia University.

NEW YORK CITY

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BY FRED S. WEINGARTEN AND BURRILL B. CROHN.

[From the Laboratory of Biological Chemistry of Columbia University, at the College of
Physicians and Surgeons, New York.]

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I. INTRODUCTION.

CHANGES in the volume or in the character of the blood affect the body more or less promptly and in some cases most profoundly. A sudden shift of a large quantity of blood, as in shock,

¹ Every effort has been made, in the preparation of this paper, to present the data of these experiments in a manner closely analogous to that of the paper in

or a direct loss of much blood, as in ordinary external hemorrhage, will cause results varying in kind and degree with the quantity and the rapidity of the change as well as the part of the body involved. Our knowledge of the effects of hemorrhage, as well as of the resultant changes in the body and in the remaining blood, is limited. A host of investigators have observed the clinical changes after both accidental hemorrhage and blood-letting, and as many have been busy with studies of the morphology of the blood, its pathological changes in the various forms of anemia, the different degrees of importance of its components, its ability to regenerate after disease, etc. In recent years the defensive capacity of the blood has been particularly studied, and much attention has been paid to conditions affecting coagulation. As stated, however, in a previous paper from this laboratory, we had until recently comparatively little information on the chemical alterations resulting from large losses of blood.²

We have endeavored to increase our knowledge of the metabolic effects of internal hemorrhage. The series of experiments described in this paper is one of a group of researches (inaugurated in 1902 by Dr. Gies and now in progress in this laboratory) on the biochemical effects of change of volume of the circulating blood, and is the fifth of the number to be reported.³ It was aimed especially to ascertain, in this series of experiments the effects of internal hemorrhage, under conditions similar to those of the earlier experiments in this laboratory on external hemorrhage, in which Dr. Gies was assisted by Drs. Hawk, White, and Hays, and Mr.

which the results of Dr. GIES's work with Drs. HAWK, WHITE, and HAYS, and Mr. SEIFERT on *external* hemorrhage were described by Dr. GIES (see HAWK and GIES: This journal, 1904, xi, p. 171). Direct comparison of the results of the two investigations is thus rendered very easy.

A preliminary report of this work appeared in the Proceedings of the Biological Section of the American Chemical Society in affiliation with Section C of the American Association for the Advancement of Science, New York meeting, December, 1906. WEINGARTEN: Science, 1907, xxv, p. 456.

² GIES: American medicine, 1904, viii, p. 185.

³ GIES: *Ibid.*, p. 155; POSNER and GIES: Proceedings of the American Physiological Society: This journal, 1904, x, p. xxxi; HAWK and GIES: *Ibid.*, 1904, xi, p. 171; MEYER and GIES: Proceedings of the Society for Experimental Biology and Medicine, 1904, i, p. 44; WEINGARTEN: Proceedings of the Biological Section of the American Chemical Society, Science, 1907, xxv, p. 456.

Seifert.⁴ Our experiments were accordingly made closely parallel to those described by Dr. Gies in the paper on external hemorrhage.

The problem in this research, intimately connected as it is with questions related to external hemorrhage, was viewed largely from the standpoint of the physician. We kept in mind particularly internal hemorrhages resulting from ectopic gestation, and from trauma causing laceration of intra-abdominal organs. Given such hemorrhage, and the surgical interference necessitated thereby, shall the blood be allowed to remain in the peritoneal cavity, and, if so, with what results to the organism? The observations made in our attempt to throw light upon these matters covered the physical as well as chemical changes in our subjects.

II. PLAN AND METHODS OF THE EXPERIMENTS.

Scope. — We have been obliged, for lack of time and opportunity, to confine our attention almost wholly, in this study of the effects of internal hemorrhage, to the metabolism of nitrogen, sulphur, and phosphorus. The extent and number of our observations have doubtless been sufficient, however, to permit correct interpretation of our data.

Precautions. — Care in the selection and the treatment of our animals, regularity in the feeding and in the period terminations, and adequate control precautions were rigorously observed. It may be specially stated, in connection with this last point, that all our recorded analytic data represent averages of closely agreeing results obtained by us independently.

Methods. — Our metabolism work was conducted on two dogs by the various methods usually employed in, and previously described in papers from, this laboratory.⁵

Animals and environment. — The animals, two healthy, full-grown dogs, were selected with a view to their withstanding the strain of long confinement and numerous hemorrhages; nervous or delicate animals would have been useless. The dogs were kept in cages particularly well adapted for this work.⁶

⁴ HAWK and GIES: This journal, 1904, xi, p. 171.

⁵ GIES and collaborators: Biochemical researches, 1903, i, pp. 69 and 419 (Reprints 1 and 21); also HAWK and GIES: *Loc. cit.*

⁶ GIES: This journal, 1905, xvii, p. 403.

Food. — The food consisted of a mixed diet of hashed lean beef, cracker meal, lard, bone ash, and water. The raw meat was preserved in a frozen condition.⁷ The commercial cracker meal was kept dry in well-closed jars. Lard was obtained in small quantities at a time, so that a supply of fresh material would always be available. The bone ash consisted of the thoroughly incinerated, carbon-free, commercial product. Its advantages in such experiments, for regulation of the consistency of the feces, have recently been indicated in some detail.⁸ Ordinary tap water was taken.

In each of our experiments the dog was given his daily food at 10 A. M. The solids and water were well mixed. The mixture was always promptly eaten, even after the last hemorrhages of each experiment.

Periods, weights. — In the records of our experiments each day ended at 10 A. M., when the weight was taken just before giving the food. Our figures for weight represent the weight of the animal at the *end* of each day of record. We did not attempt to bring the dogs into nitrogenous equilibrium after each hemorrhage, but noted changes following each hemorrhage, whatever the plane of nutrition happened to be. Each of the dogs, however, was kept under preliminary observation and brought to constant body-weight as well as practical nitrogenous equilibrium before the beginning of the normal or prehemorrhage period. The data of this normal period of constant body weight and approximate nitrogenous equilibrium furnished the basis for estimating the changes after new conditions were effected.

Anæsthesia. — Internal hemorrhage in these experiments was brought about indirectly. Blood in known volume was taken from a femoral artery and directed without loss into the peritoneal cavity through a small abdominal incision. Each of our surgical operations for such production and control of internal hemorrhage was conducted on the animal while it was under *general* though very light anæsthesia inaugurated with ether-chloroform mixture.⁹ We sought to duplicate, in this connection, the anæsthetic conditions that

⁷ GIES: This journal, 1901, v, p. 235; Biochemical researches, 1903, i, p. 69 (Reprint 1).

⁸ GIES: Proceedings of the American Physiological Society, 1903. This journal, 1904, x, p. xxii; also STEEL and GIES: This journal, 1907, xx, p. 343.

⁹ The chloroform was added in order to shorten the preliminary struggle in opposition to the administration of the ether.

prevailed in the analogous experiments by Hawk and Gies, and postponed for future study, by Dr. Gies, the effects of internal hemorrhage in animals under the influence of a *local* anæsthetic.

Two questions naturally arose at the outset in this connection, — one regarding the probable metabolic influence of the anæsthetic, another relative to the possible effects of the necessary wounds in the hemorrhage operations. It was Dr. Gies's opinion, based upon his observations under similar conditions in this laboratory during the past half-dozen years (some of which were recorded in his paper with Dr. Hawk), that the measurable metabolic effects of light anæsthesia as planned for and conducted in these experiments could not be very decided, — that at most the metabolic effects would be relatively slight and transient. Furthermore, we were advised by Dr. Gies of the impossibility of perfectly checking the influence of general anæsthesia, whatever it might be, in work of this kind, because of the fact that the responsiveness of a dog necessarily changes during the progress of a hemorrhage experiment, *i. e.*, that "control" data obtained at the beginning, for example, would probably not apply strictly to the animal at the end of the experiment and *vice versa*. Anæsthesia itself would doubtless ordinarily change somewhat the responsiveness of an animal to repetitions of anæsthetic influences.

The weight of the evidence bearing on this question favors the conclusion that general anæsthesia, either with ether or with chloroform or with both, in normal dogs, causes increased excretion of nitrogenous matter in the urine, at least for a short time after the anæsthetic period. In an experiment by Hawk and Gies *light* ether anæsthesia¹⁰ of a dog that had been subjected a week previously to external hemorrhage (2.93 per cent of body weight) caused slightly *decreased* excretion of nitrogenous and sulphur-containing products in the urine, but had no appreciable effect on phosphorus excretion. In a second dog under similar conditions practically the same result was obtained for nitrogenous excretion. Instead, however, of aiming to check the effects of the anæsthetic on each animal, we sought rather to conform so far as possible with the anæsthetic conditions of the experiments by Hawk and Gies, in the expectation that such a course would yield comparative data that could be interpreted without confusion. We think such has been the case.¹¹

¹⁰ Inaugurated with ether-chloroform mixture.

¹¹ Shortly after this paper had been prepared for publication, an excellent paper on this subject by Dr. HAWK appeared in the Journal of biological chem-

Surgical operations. — The probable metabolic effects of the purely surgical procedures, like those of anæsthesia, may not be ignored in work of this kind, yet such influences cannot be ascertained any more precisely than those exerted by anæsthesia in experiments of the kind described here. In the experiments by Hawk and Gies there appeared to be slightly increased catabolic effects after anæsthesia and operation combined, but the effects noted were comparatively minor. In this respect, as in the case of anæsthesia, we duplicated so far as possible the conditions in the experiments by Hawk and Gies, so that our results could be checked by theirs, and believed, furthermore, that the hemorrhage results would either be decided enough to bury the minor effects of anæsthesia or operation, or both, or would be so slight as to make impossible any conclusions one way or the other. These deductions seem to have been entirely warranted.

Our surgical operations were conducted under approved methods and were begun between 2 and 3 P.M.¹² The animal was brought quickly under general anæsthesia with a minimum amount of struggling. A small branch of a femoral artery was isolated, clamped, and a cannula inserted. The leg was then covered with a sterile cloth that was kept wet with warm physiological saline solution,

istry (1908, iv, p. 321). In continuation of the research suggested by Dr. GIES, and which Dr. GIES and Dr. HAWK accordingly began together in this laboratory, Dr. HAWK has reported effects of anæsthesia on the excretion of nitrogen in the urine of several dogs in nitrogenous equilibrium. Dr. HAWK states that increased excretion of nitrogen occurred in each case during the first twenty-four to forty-eight hours after the inauguration of anæsthesia. As a rule, the immediate increase was relatively slight. The "ultimate influence" of ether anæsthesia in six of the nine experiments (5 dogs) was an increase in the urinary output of nitrogen, but in three of the nine there was a decrease in the amount of excreted nitrogen. Fæcal elimination of nitrogen was not affected. Dr. HAWK concludes his paper as follows: "The data from our experiments would seem to indicate that, in all metabolism experiments upon dogs where the animal is subjected to ether anæsthesia, it is necessary to make check experiments to determine as accurately as possible the influence of such anæsthesia and to make the proper correction. At the same time our results further indicate that the possibility of determining what the exact influence of the narcosis was during the experiment proper, by a check test either before or after such experiment, is rather remote, inasmuch as the reaction of the animal to the anæsthetic will vary at the second administration of the anæsthetic from that observed as the result of the first narcosis."

¹² Operation at this hour occurred sufficiently long after feeding to minimize gastric discomfort from anæsthesia, but allowed time for recovery and rest before the next feeding.

while further preparations for the controlled hemorrhage were under way. Similar operations were performed upon each leg on several occasions. Consequently incision was made each time just above the place of previous entrance. The abdomen was opened with the usual precautions, and, after the first operation, in such a way as to avoid previous points of entrance. After about the fourth operation this was not an easy task. Similarly, it was increasingly difficult to find a satisfactory small artery in the leg, as adhesions, thrombi, and anastomoses obliterated anatomical landmarks.

With the abdomen open, blood was drawn from the artery and collected in a warm, sterile, graduated beaker. After the first operation we weighed the blood before pouring it into the peritoneal cavity, but increasing coagulation rates subsequently made it necessary for us to be satisfied with known volumes, from which the weights could be approximately calculated. At each hemorrhage we drew fairly rapidly a quantity of blood equal to from $2\frac{1}{2}$ per cent to $5\frac{1}{2}$ per cent of the weight of the dog as recorded at the beginning of the day of operation. As was the case in the work by Hawk and Gies, we experienced increasing difficulty in getting a free blood-flow toward the end of each operation, even when a relatively large vessel had been opened. This was due to the cumulative coagulability of the blood under the conditions of the hemorrhages and also to decreased blood-pressure. When the drawn blood clotted before it could be poured into the abdomen, as it did on several occasions, it was inserted *en masse* into the cavity and the serum poured after it. In two cases we tried to direct blood into the peritoneal cavity through a cannula introduced with a trocar. The first portion went in readily, but coagulation rapidly set in, and we introduced the remaining blood through the usual abdominal opening.

Although relatively large quantities of blood were drawn, the dogs were kept alive by our skilled anæsthetist, Mr. Christian Seifert, assistant in this laboratory.

The artery was ligated above and below the opening in it. The abdominal wall was sutured, layer by layer. Chromicized catgut was used for deep sutures, sterile thread for skin sutures. At first the wounds were covered with sterile pads kept in place by adhesive plaster. In later operations, however, a sterile dressing and colodion were found sufficient, the dog taking excellent care of the wound after the dressing came off, as it always did within two days. Drainage was slight. All the wounds healed rapidly.

At no time was there any appreciable blood-loss, either in operating or transferring. At the beginning of each anæsthesia some urine was eliminated, but as we were prepared for such emergencies, it was always caught. The lengths of the operation periods were about the same as those in the experiments by Hawk and Gies.

The dogs recovered very promptly after the operations, except the last in each experiment. There was slight vomiting in several instances, but the animal promptly took the vomitus again without reluctance.

Ligating the arteries of the leg did not seem to cause either local or general reactions.¹³ The vascular conditions were soon re-established, apparently, and at each operation we found scar tissue at the site of the previous one, with satisfactory anastomoses. There was no appreciable difference in the warmth of the legs.

Collection of excreta. — The urine was collected as voided, and was preserved in stoppered bottles with powdered thymol. The volume for each twenty-four hours was ascertained and recorded in the tables.

The addition of bone ash¹⁴ to the diet increased the bulk of the fæcal matter, but made its discharge more frequent and regular. The fæces had the usual consistency and appearance of excrement passed by dogs on a diet containing bone. There was no diarrhœa, the fæces did not stick to the cage and could be easily dried and powdered. The fæces were promptly dried on a water-bath, and the daily quantity bottled after its weight, consistency, etc., had been noted. For analysis the fæces were powdered and sieved to eliminate hair. The bone ash made all this easy. At the end of each period, and before returning the dog to the cage, the latter was cleaned. The washings were analyzed. The analytic data for cage washings were added to the figures for urinary period totals.

Analytic methods. — Nitrogen, sulphur, and phosphorus were quantitatively determined in the ingredients of the food, and also in the urines and fæces. Only pure reagents were used. The urine was also examined clinically, from time to time, especially immediately after operations, for albumin and sugar.

All determinations of nitrogen were made by the Kjeldahl process.

¹³ See also HAWK and GIES: *Loc. cit.*

¹⁴ GIES: Proceedings of the American Physiological Society, 1903. This journal, 1904, x, p. xxii; also STEEL and GIES: *Ibid.*, 1907, xx, p. 343.

Oxidation was effected with concentrated sulphuric acid, aided by a little cupric sulphate. The acid decompositions were continued for an hour after the mixtures became colorless, in conformity with the custom in this laboratory.

Total sulphur and phosphorus were determined by the customary fusion processes. Specific gravity of urine and blood was determined approximately by a hydrometer.

III. FIRST EXPERIMENT.

Animal. — The animal used in the first experiment was a mongrel bitch, plump and vigorous, weighing a little over 8 kilos.

Diet. — The character of the diet and the daily quantity were the same throughout the experiment. Data in this connection are given in Table I.

TABLE I.
COMPOSITION OF THE DAILY DIET.¹

	Hashed lean beef.	Cracker meal.	Lard.	Bone ash.	Water.
	gm.	gm.	gm.	gm.	c.c.
Daily amounts	128.0000	32.0000	24.0000	8.0000	320
Nitrogen . . .	4.7160	0.4960	0.0062	0.0024	
Sulphur . . .	0.3644	0.0419	0.0072	0.0048	
Phosphorus .	0.2880	0.0430	0.0206	1.4232	

	Weight.	Nitrogen.	Sulphur.	Phosphorus.
	gm.	gm.	gm.	m.
Totals for each daily mixture	512	5.2206	0.4183	1.7748

¹ Several lots of meat were used. These were found to vary so slightly in composition that, for purposes of computation, an average was taken of the various analyses (HAWK and GIES, *Loc. cit.*). As the dogs were not kept in perfect nitrogenous equilibrium, this course did not materially affect our deductions.

Preparatory period. — A preparatory period of twelve days, which brought the animal to the desired condition, was terminated on February 4 (1906) at 10 A. M. The dog then weighed 8.12 kilos. At this point the accumulation of analytic data was begun. The experiment continued without interruption until April 5, a period of sixty-one days, and terminated with the death of the dog on

the operating-table, as we were about to start a new hemorrhage period. The sixty-one days were divided into one period of normal conditions, with the animal in practical nitrogenous equilibrium, and five post-hemorrhagic periods.

First period. Normal conditions. Maintenance of approximate nitrogenous equilibrium. Days, 1-5; February 4-8, 1906. — Approximate equilibrium was maintained and a basis for subsequent comparisons afforded.

Second period. First hemorrhage. Days, 6-21; February 9-24. — On the sixth day we operated as previously described, trying at first to utilize a very small branch of a femoral artery. After many attempts we selected a somewhat larger one, the main saphenous branch, and inserted the cannula. A one-inch incision into the abdomen was made in the median line, just below the xiphoid. The blood was poured into a warm funnel connected with a rubber tube, and conveyed directly into the peritoneal cavity.

Schedule of operations. — Anæsthesia started, 2.20 P. M. Operation started, 2.45. Cannula in artery, 3.24. Abdomen opened, 3.40. Blood drawn, 3.45. Blood in peritoneal cavity, 3.47. Abdomen closed, 4.10. Anæsthetic discontinued, 4.20. Leg closed and bandaged, 4.30. Dog up, 4.45.

Blood. — The quantity of blood transferred was 231 gm., an amount equal to 2.85 per cent of the dog's weight (8.09 kg.) at the beginning of the period.

Third period. Second hemorrhage. Days, 22-33; February 25-March 8. — Operation was started as before, but on the other leg. Preliminary difficulty with a very small arterial branch, as before, again necessitated the use of a larger one. Having cannulized the saphenous artery, a trocar and cannula were pushed through the left rectus, and wrapped about with cloth dipped in hot physiological saline solution. The drawn blood clotted before it could be completely poured through the cannula. Thereupon the usual abdominal incision was made, this time through the left rectus, so as to include the opening made by the trocar. The clot and serum were then passed into the peritoneal cavity, which was closed without further incident. The dog vomited slightly during the night, and some of this was admixed with a fraction of the urine. On filtering, however, a fair separation was made, and the vomitus added to the diet for that day.

Schedule of operations. — Anæsthesia started, 2.45 P. M. Operation started, 3.14. Artery exposed, 3.21. Trocar in abdomen, 3.53. Abdomen opened, 4.00. Blood in abdomen, 4.20. Abdomen closed, 4.55. Anæsthetic discontinued, 5.00. Leg closed, 5.18. Dog up, 5.25.

Blood. — The quantity of blood transferred was 245 gm., an amount equal to about 3.15 per cent of the weight of the animal at the commencement of the period.

Fourth period. Third hemorrhage. Days, 34-42; March 9-17. — Operation was started as usual. A femoral artery was entered at a point as far distally as possible. When the blood had been drawn, its coagulation was so rapid that our usual small abdominal incision was insufficient and had to be lengthened about half an inch to admit the clots, which were pressed through the opening and followed by the serum. The animal vomited slightly toward evening, but the ejected material was successfully caught. It was promptly eaten by the animal. The extreme hemorrhage was the feature of this operation. Blood was drawn until the animal showed extreme cardiac distress. The dog recovered promptly, however, and was lively and well during the entire period.

Schedule of operations. — Anæsthesia started, 2.15 P. M. Operation started, 2.45. Artery exposed, 3.00. Abdomen opened, 3.02. Anæsthetic discontinued, 3.05. Blood drawn, 3.07. Blood in abdomen, 3.15. Abdomen closed, 3.42. Leg closed, 4.00. Dog up, 4.10.

Blood. — The quantity of blood transferred was 340 grams, an amount equal to about 4.31 per cent of the weight of the animal at the opening of the period.

Fifth period. Fourth hemorrhage. Days, 43-52; March 18-27. — Operation was started by exposing a femoral artery as far distally as possible. The abdomen was opened on the right side by a Kammerer incision. On account of scars and adhesions the incision had to be made an inch and a half long. Extreme care had to be taken in closing the abdomen on account of the before-mentioned fibrosis. The deep layers were closed with fine interrupted catgut sutures, the fascia and skin with silk. A three-inch adhesive band retaining a sterile pad was put about the body. The plan had been to exceed the amount of the previous hemorrhage, but heart beat and respiration, as well as blood-pressure, were at such a low ebb that we were unable to do so. Rapid blood-clotting was a feature. In spite of the conditions that prevailed, recovery was prompt.

Schedule of operations. — Anæsthesia, 2.18 P. M. Leg opened, 2.38. Artery cannulized, 2.47. Abdomen opened, 3.06. Blood drawn, 3.12. Blood into abdomen, 3.25. Abdomen closed, 4.26. Leg closed, 4.40. Anæsthetic discontinued, 4.20. Dog up, 4.30.

Blood. — The quantity of blood transferred was 260 grams, an amount equal to about 3.5 per cent of the dog's weight at the opening of the period.

While the dog was bright she was very much weakened, and recovery from the immediate effects of operation was less prompt than before. All food was as promptly eaten as at first, however.

Sixth period. Fifth hemorrhage. Days, 53-61; March 28-April 5. — Operation was conducted as usual. The femoral artery was entered as far distally as possible, and the abdomen was opened in the same way as for the previous hemorrhage but on the opposite side. Owing to specially rapid clotting, the blood had to be drawn and introduced intraperitoneally in three separate portions. Blood was drawn to the limit of the dog's endurance.

Schedule of operations. — Anæsthesia started, 2 P. M. Leg opened, 2.21. Artery cannulized, 2.30. Abdomen opened, 2.34. Blood drawn and into abdomen, 2.38 to 2.41, 2.41 to 2.52, 2.52 to 2.57. Abdomen closed, 3.20. Leg closed, 3.30. Anæsthetic discontinued, 3.50. Dog up, 4.00.

Blood. — The quantity of blood transferred was 250 grams, an amount equal approximately to 3.54 per cent of the dog's weight at the opening of the period.

The dog showed seriously the drain upon the system. She seemed to be recovering gradually throughout the period (days 53-61), but was on a very low plane of vitality even at the end, as evidenced by sudden death, probably from shock just before bleeding at the close of the sixth operation, which was conducted in the usual way on the sixty-second day.

Autopsy. — There was no free fluid in the abdomen. The organs presented an appearance of extreme anæmia. Heart and lungs were normal. In life the gums and tongue of the animal had been pale after the third operation. The abdominal viscera were free from adhesions. The omentum was not discolored.

Supplementary data. Periods I-VI. — The room temperature averaged about 21° C. Respiration and blood-pressure during the operations varied with the amount of blood drawn, the rapidity of the hemorrhage, and the condition of the animal.¹⁶ In the later operations cardiac and respiratory distress became evident much sooner than in the earlier ones. There was always a slight increase of pulse rate for about twenty-four hours after the operation, with irregular action for about the same time after the last operation. Simultaneously there was increased respiration. Pulse and respiration rates were practically normal after about forty-eight hours. Temperature was slightly elevated at the beginning of each hemorrhage period. The secretion of saliva during the anæsthesia periods was relatively abundant at first, as is usual during light

¹⁶ DAWSON: This journal, 1900, iv, p. 6.

ether anæsthesia, but with increasing anæmia salivary secretion decreased. As a rule, the urine was acid to litmus. Immediately after hemorrhage (anæsthesia?) the urine was amphoteric to litmus. It never became markedly alkaline to that indicator. There was very little edema connected with any of the operations; the local reactions were very slight, and the dog seemed to suffer no particular discomfort because of them. With each operation the condition of anæmia became more evident.

Neither albumin nor sugar was present in abnormal quantity in any of the urines.

Analytic results. — Summaries of the results of the first experiment are given in Tables II–XI.

Discussion of results. *Decline in body weight.* — In the experiments by Hawk and Gies there was, naturally, a fall in body weight after each external hemorrhage, owing very largely to the actual abstraction of material from the body. The total loss of weight at the end of eighty-five days, after five hemorrhages, was 25 per cent. Our dog lost weight constantly and fairly steadily. There was a slight loss during the ante-operative period. The decrease was chiefly post-operative, however. There were appreciable gains at the ends of several periods upon the figures of the first few days of the corresponding periods. The total loss in weight, after five internal hemorrhages, was 11 per cent, or less than half of that noted by Hawk and Gies after five *external* hemorrhages. Much of the loss in our experiments, as in those by Hawk and Gies, was doubtless due to the direct effects of the anæsthetic.

Fluctuations in the volume of urine. — In general, as was noted by Hawk and Gies, for external hemorrhage, there was decreased elimination of urine on the day of operation, but increased excretion on the second or third day afterwards (Table III). The day of maximum urine output varied from the second to the ninth day. In the sixth period, however, there was an apparent exception, the output of urine on the day of operation having been the highest for the period, *i. e.*, 330 c.c. in comparison with 235 c.c. on the preceding day. On the day before the operation, however, there was an accidentally low elimination. A fraction of the urine belonging to that day was undoubtedly excreted with the volume passed on the day of operation (fifty-third). The average daily elimination of urine generally decreased after each hemorrhage except the last.

TABLE II (continued).

Fourth period. — Effects of operation and third hemorrhage (4.31 per cent). March 7-17, 1906.							
DAY.	Body weight.	URINE.					Fæces dry.
No. in the experiment.		Volume.		Sp. gr.	Nitrogen.		
		Daily.	Period av. to date.		Daily.	Period av. to date.	
	kilos.	c.c.	c.c.		gm.	gm.	gm.
34	7.39	235		1.026	4.55		5
35	7.48	352	293	1.017	6.28	5.41	10
36	7.38	245	277	1.014	3.27	4.70	25
37	7.39	270	275	1.022	6.13	5.07	19
38	7.43	250	270	1.020	3.23	4.69	16
39	7.46	225	262	1.015	3.25	3.91	7
40	7.48	330	272	1.017	5.47	4.60	12
41	7.51	295	275	1.018	4.66	4.61	12
42	7.50	290	277	1.016	4.58	4.60	14

Fifth period. — Effects of operation and fourth hemorrhage (3.57 per cent). March 18-27, 1906.							
43	7.35	210		1.020	2.82		11
44	7.35	310	260	1.022	7.32	5.07	12
45	7.26	275	265	1.014	3.85	4.66	21
46	7.35	225	255	1.018	4.21	4.55	15
47	7.35	270	258	1.020	5.20	4.68	13
48	7.36	255	257	1.017	4.65	4.68	12
49	7.48	264	258	1.018	4.85	4.76	11
50	7.38	316	265	1.020	5.90	4.85	4
51	7.37	325	272	1.017	4.91	4.86	8
52	7.40	235	268	1.014	3.33	4.71	8

Sixth period. — Effects of operation and fifth hemorrhage (3.54 per cent). March 28-April 5, 1906.							
53	7.22	330		1.025	7.12		29
54	7.20	307	318	1.020	3.88	5.50	14
55	7.10	290	309	1.018	5.14	5.38	19
56	7.17	260	296	1.018	4.93	5.27	11
57	7.18	245	286	1.020	4.67	5.15	16
58	7.19	267	283	1.016	3.45	4.87	20
59	7.20	287	283	1.018	4.95	4.88	15
60	7.21	305	286	1.017	4.70	4.85	8
61	7.21	305	288	1.017	4.70	4.84	16

TABLE III.

TOTAL URINE VOLUMES ON THE EARLIER DAYS OF THE PERIODS.

Conditions.	Period no.	First day.	Second day.	Third day.	Fourth day.
Normal	I	310	300	320	310
First hemorrhage . .	II	245	270	295	240
Second hemorrhage .	III	200	360	255	270
Third hemorrhage .	IV	235	352	245	270
Fourth hemorrhage .	V	210	310	275	225
Fifth hemorrhage .	VI	330	307	290	260

TABLE IV.

ANALYTIC TOTALS AND AVERAGES FOR NITROGEN IN EACH PERIOD.

Period number	I 5	II 16	III 12	IV 9	V 10	VI 9
Days in the period . .						
Conditions of the period .	Normal.	{ First hemor.	Second hemor.	Third hemor.	Fourth hemor.	Fifth hemor.
	gm.	gm.	gm.	gm.	gm.	gm.
Food	26.10	83.52	62.64	46.98	52.20	46.98
Excreta	25.53	89.43	64.94	43.06	50.45	46.50
Total balance	+ 0.57	- 5.91	- 2.30	+ 3.92	+ 1.75	+ 0.48
Average daily balance .	+ 0.11	- 0.37	- 0.19	+ 0.43	+ 0.17	+ 0.05

TABLE V.

NITROGEN IN THE URINE, PER PERIOD.

Period number	I 5	II 16	III 12	IV 9	V 10	VI 9
Days in the period . .						
Conditions of the period .	Normal.	{ First hemor.	Second hemor.	Third hemor.	Fourth hemor.	Fifth hemor.
	gm.	gm.	gm.	gm.	gm.	gm.
Daily average	4.80	5.25	5.14	4.60	4.71	4.84
Average, first three days	4.95	5.03	5.00	4.70	4.66	5.38
Average, last three days	4.82	4.63	5.24	4.90	4.71	4.78

TABLE VI.
NITROGEN IN THE FÆCES, PER PERIOD.

Period number	I	II	III	IV	V	VI
Days in the period . . .	5	16	12	9	10	9
Conditions of the period .	Normal.	{ First hemor.	Second hemor.	Third hemor.	Fourth hemor.	Fifth hemor.
	gm.	gm.	gm.	gm.	gm.	gm.
Total	1.50	4.55	3.19	1.37	3.37	2.92
Daily average	0.30	0.28	0.26	0.15	0.33	0.32

TABLE VII.
QUANTITATIVE FÆCAL ELIMINATIONS, PER PERIOD.

Period number	I	II	III	IV	V	VI
Days in the period . . .	5	16	12	9	10	9
Conditions of the period .	Normal.	{ First hemor.	Second hemor.	Third hemor.	Fourth hemor.	Fifth hemor.
	gm.	gm.	gm.	gm.	gm.	gm.
Dry weight: period total	70	228	175	120	115	148
" " daily average	14	14	15	13	12	16

TABLE VIII.
SUMMARY OF ANALYTIC DATA FOR TOTAL SULPHUR AND PHOSPHORUS
METABOLISM.

Period.		SULPHUR.				PHOSPHORUS.			
		Total.		Balance.		Total.		Balance.	
No.	Conditions.	In- gested.	Ex- creted.	Total.	Daily Average.	In- gested.	Ex- creted.	Total.	Daily Average.
I	Normal	gm. 2.09	gm. 1.71	gm. +0.38	gm. +0.0760	gm. 8.87	gm. 8.34	gm. +0.57	gm. +0.1140
II	First hemor.	6.69	5.27	+1.42	+0.0887	28.39	21.71	+6.68	+0.4175
III	Second "	5.01	4.44	+0.57	+0.0475	21.29	24.12	-2.83	-0.2358
IV	Third "	3.76	3.16	+0.60	+0.0666	15.97	13.77	+2.20	+0.2440
V	Fourth "	4.18	2.86	+1.32	+0.1320	17.74	12.57	+5.17	+0.5170
VI	Fifth "	3.76	3.64	+0.12	+0.0133	15.97	19.20	-3.23	-0.3580

Specific gravity of the urine. — This varied from 1.011 to 1.026. It generally increased on the day of hemorrhage, contrary to what

TABLE IX.
QUANTITATIVE SULPHUR EXCRETION, PER PERIOD.

Period number	I 5	II 16	III 12	IV 9	V 10	VI 9
Days in the period		{ First	Second	Third	Fourth	Fifth
Conditions of the period . .	Normal.	hemor.	hemor.	hemor.	hemor.	hemor.
Urine	gm. 1.43	gm. 4.38	gm. 3.76	gm. 2.67	gm. 2.31	gm. 3.00
Fæces	0.284	0.89	0.686	0.493	0.545	0.639
DAILY AVERAGES.						
Urine	0.28	0.27	0.31	0.29	0.23	0.33
Fæces	0.056	0.055	0.057	0.054	0.054	0.071

TABLE X.
QUANTITATIVE PHOSPHORUS EXCRETION, PER PERIOD.

Period number	I 5	II 16	III 12	IV 9	V 10	VI 9
Days in the period		{ First	Second	Third	Fourth	Fifth
Conditions of the period . .	Normal.	hemor.	hemor.	hemor.	hemor.	hemor.
Urine	gm. 1.04	gm. 4.14	gm. 3.12	gm. 2.49	gm. 2.48	gm. 2.60
Fæces	7.30	17.57	20.99	13.89	10.99	16.60
DAILY AVERAGES.						
Urine	0.20	0.25	0.26	0.27	0.24	0.28
Fæces	1.46	1.09	1.74	1.54	1.09	1.84

our predecessors found for external hemorrhage. In the third period there was no change in this respect on the day of operation, although the fall in urinary volume was very sharp.¹⁷ While fluctu-

¹⁷ Practically all of the volume for the day was eliminated before the operation, however.

ating considerably, specific gravity was generally lowest at the ends of hemorrhage periods. The maximum figure for specific gravity was recorded on the fourth day in the second period, on the fifth day in the third period, on the first day in the fourth period, on the second day in the fifth period, and on the first day in the sixth period. The changes were not regular enough to warrant any general deduction regarding their significance.

Nitrogen catabolism. — Elimination of urinary nitrogen was increased during the first few days of each hemorrhage period. After the first and last hemorrhages such increases occurred on the first

TABLE XI.

SUMMARY OF PERIOD, AVERAGE DAILY BALANCES FOR NITROGEN, SULPHUR, AND PHOSPHORUS.

Period number	I	II	III	IV	V	VI
Conditions of the period . .	Normal.	{ First hemor.	Second hemor.	Third hemor.	Fourth hemor.	Fifth hemor.
	gm.	gm.	gm.	gm.	gm.	gm.
Nitrogen	+0.110	-0.370	-0.190	+0.430	+0.170	+0.050
Sulphur	+0.076	+0.089	+0.048	+0.067	+0.132	+0.013
Phosphorus	+0.114	+0.418	-0.236	+0.244	+0.517	-0.358

day; after the remaining hemorrhages, increased elimination of urinary nitrogen took place later in the periods. Individual figures for urinary nitrogen were lower, as a rule, in the last three periods than in the first three. The average daily urinary elimination of nitrogen was higher by the end of the first two hemorrhage periods than at their beginnings. The reverse was true of the similar daily averages for the last three hemorrhage periods. The highest final daily average for a period was recorded after the first hemorrhage; the lowest, after the third hemorrhage.

Comparison of the daily average amount of nitrogen in the urine of the last three days of a period with that of the first three days of the hemorrhage period following shows an increase after hemorrhage in three of the five periods (first, second, and fifth). The daily average amount of urinary nitrogen for the whole of the second period (after the first hemorrhage) was *higher* than that for either the first or last three days of that period. In the fourth

period (after the third hemorrhage), on the other hand, the general average was *lower* than the averages for the first and last three days.

The daily average amount of faecal nitrogen per period shows a regular decrease to the fourth period, whereas the daily average amount of urinary nitrogen per period rose in the second period before decreasing regularly to the fourth period. But whereas the average daily excretion of urinary nitrogen per period was practically "normal" after the fourth period, the average elimination of nitrogen per period in the faeces was greatest in the fifth and sixth periods.

On comparing the total amounts of nitrogen ingested with those excreted it is evident that there were minus balances after the first and second hemorrhages but plus balances thereafter (Table IV).

These results suggest that after the first two hemorrhages the nitrogenous matter in the transferred blood was lost from the system in large part, either directly or indirectly,—the animal's nitrogenous surplus was apparently sufficient to meet immediate needs. It might also be inferred, however, from the results in Table IV, that the animal's nitrogenous surplus had been exhausted after the second hemorrhage, for after each of the last three hemorrhages practically all of the nitrogenous matter of the transported blood appeared to be utilized ultimately to make good the losses that ensued directly from the bodily withdrawal of blood from the circulation. These hypotheses appear to explain in the main the results of the second experiment also (see page 233). Nevertheless, it is quite probable that the influence of the anæsthetic was sufficient to make it impossible to interpret correctly the significance of the small period balances as well as the remaining results that otherwise might be attributed wholly to the effects of the hemorrhages. On the other hand, it is not very probable that the uniformities in the results of our two experiments (see page 239) are mere coincidences or due primarily to the action of the anæsthetic (see Table XI).

Sulphur catabolism.—For lack of time our quantitative determinations of sulphur in the excreta of both our experiments were confined to "period urines" and "period faeces." The period balances, as shown in Table VIII, were always small "plus balances." The daily average "plus balances" recorded in Table VIII make it apparent that the internal hemorrhages had no appreciable effect on the total sulphur catabolism per period. The records fail to show

close parallelism between the total nitrogen and sulphur outputs except in the first and last three periods (see Table XI).

The analytic data for urinary and fæcal sulphur of the first experiment are summarized in Table IX.

Phosphorus catabolism. — Our quantitative determinations of phosphorus in the excreta, as in the case of sulphur, were confined in both our experiments to "period urines" and "period fæces." The period balances, as shown in Table VIII, were plus balances in all the periods except the third and sixth. The average daily balances recorded in Table VIII indicate that the internal hemorrhages had no uniform effect on the phosphorus catabolism. The results of our analyses make it evident that total phosphorus catabolism per period was not perfectly concordant with the total catabolism of nitrogen and sulphur during the same periods. Facts in this relation are shown in Table XI.

Our analytic data for urinary and fæcal phosphorus of the first experiment are summarized in Table X.

IV. SECOND EXPERIMENT.

Animal. — The second dog was a short-haired mongrel male, not as lively as the first, but in good condition.

Diet. — The character and quantitative features of the dog's diet are indicated in Table XII. The diet was uniform throughout the entire experiment.

Preparatory period. — During a preparatory period of seven days, the dog was brought to approximate nitrogenous equilibrium, after which, on April 28 (1906), we started the period of special observations, as recorded in Table XIII. The dog then weighed 6.75 kilos. The records were continued daily for fifty-seven days. The experiment was divided into seven periods.

First period. Normal conditions. Maintenance of approximate nitrogenous equilibrium. Days, 1-7; April 28-May 4, 1906. — Weight was maintained at 6.75 kilos daily for seven days.

Second period. First hemorrhage. Days, 8-17; May 5-14. — The operation was conducted without difficulty. Blood was drawn in three portions, and at once poured into the peritoneal cavity, as in the first experiment.

Schedule of operations. — Anæsthesia started, 2.50 p. m. Leg opened, 3.10. Artery cannulized, 3.22. Abdomen opened, 3.25. Blood introduced at 3.30, 3.37, and 3.47. Abdomen closed, 4.06. Anæsthetic continued, 4.08. Leg closed, 4.15. Dog up, 4.30.

Blood. — The quantity of blood transferred was 202 grams, an amount equal to 3.88 per cent of the weight of the dog just before the operation.

Third period. Second hemorrhage. Days. 18-29; May 15-26. — The operative procedure was uneventful. Opposite sides were used for the exposures, — right leg and left side of abdomen.

TABLE XII.
COMPOSITION OF THE DAILY DIET.¹

	Hashed lean beef.	Cracker meal.	Lard.	Bone ash.	Water.
	gm.	gm.	gm.	gm.	cc.
Daily amounts . . .	105.0000	31.0000	21.0000	7.0000	280
Nitrogen	3.8690	0.4805	0.0055	0.0021	
Sulphur	0.2989	0.0406	0.0063	0.0042	
Phosphorus	0.2360	0.0415	0.0180	1.2450	
TOTALS FOR EACH DAILY MIXTURE.					
Total weight.	Nitrogen.	Sulphur.	Phosphorus.		
gm. 444	gm. 4.3570	gm. 0.3500	gm. 1.5405		

¹ Several lots of meat were used. These were found to vary so slightly in composition that, for purposes of computation, an average was taken of the various analyses (HAWK and GIES: *Lcc. cit.*). As the dogs were not kept in perfect nitrogenous equilibrium, this course did not materially affect our deductions.

Schedule of operations. — Anæsthesia started, 3.30 p. m. Artery cannulized, 3.50. Abdomen opened, 3.55. Blood introduced, 3.55, 4.00, 4.04, 4.09. Abdomen closed, 4.16. Anæsthetic discontinued, 4.16. Leg closed, 4.25. Dog up, 4.45.

Blood. — The quantity of blood transferred was 354 grams, an amount equal to 5.56 per cent of the weight of the dog just before the operation. This was the largest hemorrhage of the series and carried the dog to his cardiac and respiratory limits. The animal, as usual, recovered quickly in spite of the large quantity of blood transported.

Fourth period. Third hemorrhage. Days. 30-36; May 27-June 2. — Operation was conducted as usual, and was without incident except a little delay in closing the abdomen.

Schedule of operations. — Anæsthesia started, 4.25 P. M. Leg opened, 4.47. Artery cannulized, 5.02. Abdomen opened, 5.10. Blood drawn, 5.13, 5.16, 5.19. Abdomen closed, 5.45. Anæsthetic discontinued, 5.50. Leg closed, 6.00. Dog up, 6.20.

Blood. — The quantity of blood transferred was 232 grams, an amount equal to 3.5 per cent of the weight of the dog at the beginning of the period.

Fifth period. Fourth hemorrhage. Days, 37-40; June 3-6. — The dog was subjected to a heavy hemorrhage after but a short period for recovery from the previous transfer. Operation was without incident, but the animal required constant watching, for the cardiac action was weak. Greatly increased coagulability of the blood required withdrawal of small amounts at a time.

Schedule of operations. — Anæsthesia started, 2.15 P. M. Leg opened, 2.35. Cannula in artery, 3.02. Abdomen opened, 3.10. Blood drawn, 3.12, 3.18, and 3.25. Abdomen closed, 3.44. Anæsthetic discontinued, 3.50. Leg closed, 3.56. Dog up, 4.10.

Blood. — The quantity of blood transferred was 262 grams, an amount equal to 4.19 per cent of the dog's weight at the beginning of the period.

The dog showed the strain and was not very lively at any time during this short period.

Sixth period. Fifth hemorrhage. Days, 41-47; June 7-13. — This hemorrhage also followed a short period for recovery. The amount of blood transferred was also large, especially in view of the heavy drain upon the system that occurred four days previously. The usual operation was carried out, but it was difficult to find an artery sufficiently large in either hind leg without invading the pelvis.

Schedule of operations. — Anæsthesia started, 4 P. M. Leg opened, 4.18. Cannula in artery, 4.36. Abdomen opened, 4.45. Blood drawn, 4.48, 4.50, and 4.52. Abdomen closed, 5.13. Anæsthetic discontinued, 5.15. Leg closed, 5.24. Dog up, 5.35.

Blood. — The quantity of blood transferred was 288 grams, an amount equal to 4.66 per cent of the dog's weight at the commencement of the period.

The dog's vitality was greatly diminished by the hemorrhage.

Seventh period. Sixth and seventh hemorrhages. Days, 48-57; June 14-23.

— Two internal hemorrhages were effected on successive days, after a short period for recovery from the preceding (fifth) hemorrhage. This plan caused excessive removal of blood from the circulation and nearly resulted in the death of the animal after each transfer. It was apparent that we had carried internal hemorrhage by our method as far as it was possible to take it without

TABLE XIII.

SOME OF THE DAILY RECORDS OF THE SECOND METABOLISM EXPERIMENT.¹**First Period.** — Maintenance of approx. nitrogenous equilibrium. April 28–May 4, 1906.

Day.	Body weight.	Urine.					Fæces dry.
No. in the experiment.		Volume.		Sp. Gr.	Nitrogen.		
		Daily.	Period av. to date.		Daily.	Period av. to date.	
	kilos.	c.c.	c.c.		gm.	gm.	gm.
1	6.75	285		1.015	3.97		4
2	6.75	290	287	1.014	3.67	3.82	12
3	6.75	305	293	1.015	4.20	3.95	14
4	6.75	300	295	1.017	4.67	4.13	16
5	6.75	250	286	1.012	2.89	3.88	11
6	6.75	325	293	1.014	4.10	3.92	5
7	6.75	280	291	1.015	3.61	3.87	25

Second period. — Effects of operation and first hemorrhage (3.88 per cent). May 5–14, 1906.

8	6.62	270		1.028	5.48		5
9	6.54	400	335	1.013	5.09	5.28	7
10	6.66	205	292	1.016	3.65	4.74	31
11	6.58	210	246	1.027	4.24	4.64	18
12	6.52	225	262	1.020	4.38	4.57	19
13	6.52	260	262	1.018	4.10	4.49	11
14	6.45	300	267	1.024	6.69	4.80	16
15	6.45	220	261	1.014	3.10	4.59	0
16	6.42	220	255	1.019	4.31	4.56	8
17	6.38	285	260	1.019	5.33	4.64	20

Third period. — Effects of operation and second hemorrhage (5.56 per cent). May 15–26, 1906.

18	6.35	175		1.026	3.84		9
19	6.21	280	227	1.018	4.95	4.39	23
20	6.27	230	228	1.019	4.57	4.45	7
21	6.25	275	240	1.019	5.30	4.66	16
22	6.30	235	239	1.013	3.28	4.39	2
23	6.30	240	239	1.019	4.80	4.46	23
24	6.31	270	243	1.015	4.27	4.43	15
25	6.30	290	249	1.015	4.05	4.38	13
26	6.29	255	250	1.016	3.60	4.30	29
27	6.26	300	255	1.017	4.87	4.35	17
28	6.30	255	255	1.013	3.20	4.25	20
29	6.37	225	253	1.014	2.72	4.12	10

¹ Facts regarding the daily food are given in Table XII.

TABLE XIII (continued).

Fourth period. — Effects of operation and third hemorrhage (3.5 per cent). May 27–June 2, 1906.							
Day.	Body weight.	Urine.					Fæces dry.
No. in the experiment.		Volume.		Sp. Gr.	Nitrogen.		
		Daily.	Period av. to date.		Daily.	Period av. to date.	
	kilos.	c.c.	c.c.		gm.	gm.	gm.
30	6.28	290		1.017	4.43		16
31	6.23	320	305	1.016	4.97	4.70	14
32	6.22	310	307	1.016	4.42	4.61	8
33	6.22	300	305	1.012	3.97	4.45	2
34	6.22	265	297	1.015	3.92	4.34	17
35	6.26	300	298	1.016	5.25	4.49	10
36	6.24	295	297	1.014	4.37	4.48	14
Fifth period. — Effects of operation and fourth hemorrhage (4.19 per cent). June 3–6, 1906.							
37	6.13	195		1.024	4.23		14
38	6.12	280	238	1.010	3.56	3.89	15
39	6.20	185	220	1.012	2.27	3.35	9
40	6.17	295	239	1.018	5.56	3.91	16
Sixth period. — Effects of operation and fifth hemorrhage (4.66 per cent). June 7–13, 1906.							
41	6.14	255		1.023	5.07		17
42	6.14	250	250	1.019	4.47	4.77	16
43	6.12	315	273	1.014	4.46	4.67	3
44	6.12	230	262	1.017	4.45	4.61	11
45	6.10	310	272	1.015	4.76	4.64	16
46	6.07	270	271	1.018	4.62	4.64	17
47	6.09	210	263	1.013	2.71	4.36	21
Seventh Period. — Effects of operation and sixth and seventh hemorrhages (1.6 per cent and 1.8 per cent). June 14–23, 1906.							
48 ¹	5.95	310		1.018	4.56		20
49 ²	5.90	260	285	1.031	6.19	5.37	0
50	5.83	195	255	1.023	3.95	4.90	22
51	5.77	290	264	1.014	3.83	4.63	30
52 }	5.77	480	256	1.016	7.45	4.33	46
53 }							
54 }	5.78	470	251	1.016	6.48	4.06	34
55 }							
56 }	5.85	550	256	1.014	6.25	3.87	46
57 }							
¹ Sixth hemorrhage, 1.6 per cent.				² Seventh hemorrhage, 1.8 per cent.			

killing the dog. It seemed probable also that metabolic effects of internal hemorrhage, if measurable ones ensued, would be at their maximal points. The operations were difficult because both legs had been worked over so much that operative fields were scarce; besides the blood coagulated with special readiness.

Schedule of operations. *Sixth hemorrhage, June 14.* — Anæsthesia started, 4.10. Leg opened, 4.45. Cannula in, 5.25. Abdomen opened, 5.32. Blood drawn, 5.36, 6.17, and 6.20. Anæsthetic discontinued, 6.30. Abdomen and leg closed, 6.37. Dog up, 6.40.

Blood. — The quantity of blood transferred was 100 grams, an amount equal to 1.6 per cent of the dog's weight at the beginning of the period.

Seventh hemorrhage, June 15. — Anæsthesia started, 4.15 P. M. Leg opened, 4.25. Cannula in artery, 5.30. Abdomen opened, 5.35. Blood in, 5.40–6.00. Abdomen closed, 6.20. Anæsthetic discontinued, 6.20. Leg closed, 6.30. Dog up, 6.35.

Blood. — The quantity of blood transferred was 108 gm., an amount equal to 1.8 per cent of the weight of the dog before the operation.

As was stated above, each of these hemorrhages nearly resulted fatally. The dog remained on a low plane of vitality for several days, but, with unimpaired appetite, gained steadily. He was kept under general observation until the following December.

Autopsy. — The dog was killed when he had regained his normal weight, nearly six months after the last operation.¹⁸ The abdomen and viscera were in excellent condition; there was no free fluid, and only a slight brownish tint to the omentum. Heart and lungs, as in the first dog, were normal. The intestines were free from adhesions, but one delicate band passed from the stomach fundus to the abdominal wall, and a similar one from the liver to the right parietes. No such adhesions occurred in the dog of the first experiment.

Supplementary data. — The remarks on page 218 apply to this experiment also.

Analytic results. — Summaries of the results of the second experiment are given in Tables XIII–XXII.

Discussion of results. *Decline in body weight.* — The dog lost weight steadily after the first hemorrhage, but there were no abrupt falls and very few recoveries. The loss after fifty-seven days and seven hemorrhages was only 13 per cent of the original weight (see page 238).

¹⁸ The diet meanwhile had been practically the same as that fed daily during the experiment.

Fluctuations in the volume of urine. — As in the previous experiment, urine output was low at first, rising to the maximum usually on the second day. In the last period the highest output occurred on the first day, as was the case after the last hemorrhage of the first experiment, and probably for identical reasons.

TABLE XIV.

TOTAL URINE VOLUMES ON THE EARLIER DAYS OF THE PERIODS.

Conditions.	Period no.	Volume of urine.			
		First day.	Second day.	Third day.	Fourth day.
Normal	I	c.c. 285	c.c. 290	c.c. 305	c.c. 300
First hemorrhage	II	270	400	205	210
Second hemorrhage	III	175	280	230	275
Third hemorrhage	IV	290	320	310	300
Fourth hemorrhage	V	195	280	185	295
Fifth hemorrhage	VI	255	250	315	230
Sixth and seventh hemorrhage	VII	310 ¹	260 ²	195	290
¹ After sixth hemorrhage.		² After seventh hemorrhage.			

Specific gravity of the urine. — This varied from 1.012 to 1.031. It was always immediately increased by the hemorrhages, and exhibited considerable variation, thereafter, during a period. Specific gravity was generally lowest at the ends of the hemorrhage periods.

Nitrogen catabolism. — Elimination of urinary nitrogen was increased during the first day or two of nearly all the hemorrhage periods. Individual figures for urinary nitrogen were lower, as a rule, in the last three hemorrhage periods than in the first three periods following hemorrhages. The average daily urinary content of nitrogen was always lower by the end of a hemorrhage period (except the fifth) than at its beginning. The highest final daily average for a period was recorded after the first hemorrhage; the lowest after the last hemorrhages. These final averages were not very divergent.

In all but one case (fifth period) the average daily amount of

nitrogen, in the urine of the three days opening a period after hemorrhage, was higher than the average for the three days closing the preceding period.

TABLE XV.
ANALYTIC TOTALS AND AVERAGES FOR NITROGEN IN EACH PERIOD.

Period number	I 7	II 10	III 12	IV 7	V 4	VI 7	VII 10
Days in the period . . .							
Conditions of the period	{ Nor- mal.	First hemor.	Second hemor.	Third hemor.	Fourth hemor.	Fifth hemor.	Sixth and seventh hemor.
Food	gm. 30.49	gm. 43.57	gm. 52.28	gm. 30.49	gm. 17.42	gm. 30.49	gm. 43.57
Excreta	28.98	49.32	53.91	32.58	16.80	32.55	40.86
Total balance	+1.51	-5.75	-1.63	-2.09	+0.62	-2.06	+2.71
Average daily balance . .	-0.21	-0.57	-0.13	-0.30	+0.15	-0.29	+0.27

TABLE XVI.
NITROGEN IN THE URINE, PER PERIOD.

Period number	I 7	II 10	III 12	IV 7	V 4	VI 7	VII 10
Days in the period . . .							
Conditions of the period	{ Nor- mal.	First hemor.	Second hemor.	Third hemor.	Fourth hemor.	Fifth hemor.	Sixth and seventh hemor.
Daily average	gm. 3.87	gm. 4.64	gm. 4.12	gm. 4.48	gm. 3.90	gm. 4.36	gm. 3.87
Average, first three days	3.95	4.74	4.45	4.61	3.89 ¹	4.67	4.90
Average, last three days	3.53	4.25	3.60	4.51	3.91 ²	4.03	3.16

¹ Average of the first two days (four-day period).
² Average of the last two days (four-day period).

The small output of nitrogen in the fæces increased to a maximum in the third period and fell to a minimum in the last period. There was a moderate increase in the second period, as was the case with urinary nitrogen. A further slightly increased output of fæcal nitrogen in the third period was inverse to the fall of nitrogen in the urine, while nitrogen in the urine rose and in the fæces fell in the fourth period. In the fifth period there was an excre-

tory decrease of nitrogen in both urine and fæces. Elimination of nitrogen in the fæces continued to decrease quantitatively, *per diem*, to the end of the experiment, and was at or below normal during the last two periods, whereas the urinary quantities rose above and fell below the normal figure.

TABLE XVII.
NITROGEN IN THE FÆCES, PER PERIOD.

Period number	I	II	III	IV	V	VI	VII
Days in the period . .	7	10	12	7	4	7	10
Conditions of the period	{ Nor- mal.	First hemor.	Second hemor.	Third hemor.	Fourth hemor.	Fifth hemor.	Sixth and seventh hemor.
Total	gm. 1.84	gm. 2.92	gm. 4.39	gm. 2.20	gm. 1.18	gm. 1.99	gm. 2.14
Daily average	0.26	0.29	0.36	0.31	0.29	0.28	0.21

TABLE XVIII.
QUANTITATIVE FÆCAL ELIMINATIONS, PER PERIOD.

Period number	I	II	III	IV	V	VI	VII
Days in the period . .	7	10	12	7	4	7	10
Conditions of the period	{ Nor- mal.	First hemor.	Second hemor.	Third hemor.	Fourth hemor.	Fifth hemor.	Sixth and seventh hemor.
Dry weight : period total	gm. 87	gm. 135	gm. 184	gm. 81	gm. 54	gm. 101	gm. 198
" " daily average	12	14	15	12	13	14	20

On comparing the total amounts of nitrogen per period in the food with those in the corresponding excreta (Table XV), it will be seen that the earlier hemorrhages were followed by small minus balances, the later hemorrhages (except the fifth) by small plus balances. This general result is in practical accord with the analogous outcome of the first experiment (see discussion, page 225).

Sulphur catabolism. — The changes in the excreted amounts of sulphur in urines for whole periods followed those of nitrogen in the same urines, though with relatively less variation, up to the last period, when the amount of sulphur rose as that for nitrogen fell. The decreased elimination of sulphur in the urine per day after the first hemorrhage was practically continuous to the fifth

period, after which there was a correspondingly cumulative increase to the end.

The figures for total sulphur catabolism show an extreme initial decrease. Later the period balances are very small, without showing regular effects of the hemorrhages. With two exceptions the period balances, as shown in Table XIX, were small "plus balances." The effects, if any, of the internal hemorrhages are not evident,

TABLE XIX.

SUMMARY OF ANALYTIC DATA FOR TOTAL SULPHUR AND PHOSPHORUS METABOLISM.

Period conditions.	SULPHUR.				PHOSPHORUS.			
	Total.		Balance.		Total.		Balance.	
	In-gested.	Ex-creted.	Total.	Daily average.	In-gested.	Ex-creted.	Total.	Daily average.
	gm.	gm.	gm.	gm.	gm.	gm.	gm.	gm.
I. Normal . . .	2.45	2.18	+0.27	+0.0386	10.78	10.53	+0.25	+0.0357
II. First hemor. .	3.50	3.60	-0.10	-0.0100	15.40	16.16	-0.76	-0.0760
III. Second hemor.	4.20	4.01	+0.19	+0.0158	18.48	23.50	-5.02	-0.4183
IV. Third hemor.	2.45	2.32	+0.13	+0.0186	10.78	9.92	+0.86	+0.1230
V. Fourth hemor.	1.40	1.28	+0.12	+0.0300	6.16	6.56	-0.40	-0.1000
VI. Fifth hemor. .	2.45	3.14	-0.69	-0.0985	10.78	12.45	-1.67	-0.2386
VII. Sixth and seventh hemor.	3.50	3.07	+0.43	+0.0430	15.40	25.41	-10.01 ¹	-1.0010
¹ This excessive minus balance was due largely to the greater elimination of fæces in this period. See Table XVIII.								

unless the output of sulphur was increased in variable degrees though not in sufficient amounts in more than two periods to change plus balances to minus balances. Total sulphur excretion for periods ran parallel with total nitrogen elimination for the same periods in all except the third and fourth (see Table XXII).

The analytic data for urinary and fæcal sulphur of the second experiment are summarized in Table XX.

Phosphorus catabolism. — The general trend of the output of phosphorus in the period urines was downward, there having been a sharp decrease in the second period, a partial recovery in the third and fourth periods, and then a decrease to a subnormal output in the last two periods.

TABLE XX.
QUANTITATIVE SULPHUR EXCRETION, PER PERIOD.

TOTALS.							
Period number . . .	I	II	III	IV	V	VI	VII
Days in the period . .	7	10	12	7	4	7	10
Conditions of the period	{Nor- mal.	First hemor.	Second hemor.	Third hemor.	Fourth hemor.	Fifth hemor.	{Sixth and seventh hemor.
Urine	gm. 1.82	gm. 3.03	gm. 3.211	gm. 1.98	gm. 1.00	gm. 1.99	gm. 2.14
Fæces	0.357	0.567	0.794	0.343	0.277	0.434	1.00
DAILY AVERAGES.							
Urine	0.260	0.300	0.290	0.280	0.250	0.270	0.290
Fæces	0.051	0.056	0.066	0.049	0.069	0.062	0.100

TABLE XXI.
QUANTITATIVE PHOSPHORUS EXCRETION, PER PERIOD.

Period number . . .	I	II	III	IV	V	VI	VII
Days in the period . .	7	10	12	7	4	7	10
Conditions of the period	{Nor- mal.	First hemor.	Second hemor.	Third hemor.	Fourth hemor.	Fifth hemor.	{Sixth and seventh hemor.
Urine	gm. 2.06	gm. 1.79	gm. 2.45	gm. 1.86	gm. 0.83	gm. 1.39	gm. 1.90
Fæces	8.47	14.36	21.05	8.05	5.73	11.05	23.51
DAILY AVERAGES.							
Urine	0.29	0.17	0.20	0.26	0.20	0.19	0.19
Fæces	1.21	1.43	1.75	1.15	1.43	1.58	2.35

The daily average elimination of phosphorus in the fæces decreased, as a rule, as the daily average output of phosphorus in the urine increased. The minimal excretion in the fæces of the fourth period corresponded with the maximum amount of excreted phosphorus in the urine after hemorrhage, whereas the maximum amount

of phosphorus in the fæces of the last period corresponded with the subnormal excretion of phosphorus in the urine.

The amounts of ingested phosphorus were less than those of excreted phosphorus in all but the first and fourth periods, *i. e.*, the balances, except in these two periods, were minus balances. This result is practically the opposite of that obtained in the first experiment.

TABLE XXII.

SUMMARY OF PERIOD, AVERAGE DAILY BALANCES FOR NITROGEN, SULPHUR, AND PHOSPHORUS.

Period number . . .	I	II	III	IV	V	VI	VII
Conditions of the period	Normal.	{ First hemor.	Second hemor.	Third hemor.	Fourth hemor.	Fifth hemor.	{ Sixth and seventh hemor.
	gm.	gm.	gm.	gm.	gm.	gm.	gm.
Nitrogen	+0.210	-0.570	-0.130	-1.010	+0.150	-0.290	+0.270
Sulphur	+0.182	-0.010	+0.016	+0.019	+0.030	-0.099	+0.043
Phosphorus	+0.036	-0.076	-0.418	+0.123	-0.100	-0.239	-1.001

The figures for total phosphorus catabolism indicate that phosphorus elimination ran somewhat independently of both nitrogen and sulphur excretion, except in the first, second, and sixth periods. Facts in this relation are shown in Table XXII.

Our analytic data for urinary and faecal phosphorus of the second experiment are summarized in Table XXI.

The general influence of the hemorrhages on phosphorus metabolism seems to have been in the direction of increased excretion, although the power of the anæsthetic to produce such effects must not be overlooked in an interpretation of these results.

V. DISCUSSION OF THE GENERAL RESULTS OF THE TWO EXPERIMENTS.

Decline in body weight. — The first dog lost 11 per cent after sixty-one days and five internal hemorrhages; the second dog lost 13 per cent after fifty-seven days and seven internal hemorrhages,

in comparison with a loss of 25 per cent after eighty-five days and five external hemorrhages, and 16 per cent after thirty-three days and four external hemorrhages, in the experiments by Hawk and Gies under similar feeding conditions. These facts certainly indicate that internal hemorrhage causes less drain upon the system than external hemorrhage.

Fluctuations in the volume of urine. — Tables III and XIV exhibit practically identical results, and show that the maximal volumes of urine were usually excreted on the second day after hemorrhage, in spite of the tendency of ether to cause greatly increased flow of urine on the day of anæsthesia, when anæsthesia is as light as that induced in these experiments. The outcome was evidently a resultant of the contrary immediate effects of ether anæsthesia and loss of blood from the vessels.¹⁹

Changes in the specific gravity of the urine. — Specific gravity was increased on the day of hemorrhage in each experiment, in nearly every instance, and fell with considerable fluctuation to low points at the ends of hemorrhage periods. After external hemorrhage, under similar conditions of anæsthesia, specific gravity either fell at first or was unchanged, but rose in a day or two to maximal points and declined to normal values at the ends of the periods.

Effects on the fæces. — Neither the weights (fresh or dry) of the average daily fæcal eliminations nor the corresponding fæcal contents of nitrogen, sulphur, and phosphorus varied sufficiently to show any marked influences of the hemorrhages. There was evidently no particular effect on digestion or on assimilation. There were apparently also no noticeable effects on the secretion into the alimentary tract of nitrogenous matter, such as mucus. These results accord with those of the related study of external hemorrhage.

Nitrogen catabolism. — In each of the two experiments slightly less nitrogen was eliminated than ingested during the normal period. The earlier hemorrhages were always followed by small minus period balances of nitrogen, the later hemorrhages (except in one instance) by small plus period balances of nitrogen (see Table XXIII). In a general way the total excretion of nitrogen throughout the entirety of each experiment was only slightly greater than the total amount ingested. Either ether anæsthesia or internal hemorrhage, or both, were devoid of pronounced disturbing effects

¹⁹ See HAWK and GIES: *Loc. cit.*, p. 194, Table III, for facts in this connection pertaining to the effects of anæsthesia and of external hemorrhage.

on the general metabolism of the dogs in these experiments, as measured by us, or their influences were mutually antagonistic in the main and therefore not discernible for more than a day or two, if at all.

TABLE XXIII.

ANALYTIC TOTALS OF NITROGEN FOR ALL THE PERIODS OF EACH EXPERIMENT.

Period No.	FIRST EXPERIMENT.		SECOND EXPERIMENT.	
	Nitrogen in food.	Nitrogen in excreta.	Nitrogen in food.	Nitrogen in excreta.
	gm.	gm.	gm.	gm.
I	26.10	25.53	30.49	28.98
II	83.52	89.43	43.57	49.32
III	62.64	64.94	52.28	53.91
IV	46.98	43.06	30.49	32.58
V	52.20	50.45	17.42	16.80
VI	46.98	46.50	30.49	32.55
VII			43.57	40.86
Total	318.42	319.91	248.31	255.00
Total balance . . .	- 1.49		- 6.69	
Average daily balance	- 0.024		- 0.117	

Elimination of urinary nitrogen was greater during the first day or two of practically all the hemorrhage periods. Individual figures for urinary nitrogen were lower, as a rule, in the last three hemorrhage periods than in the first three periods after hemorrhages. The average daily urinary elimination of nitrogen was usually lower by the end of a hemorrhage period than at its beginning. The highest daily average content of nitrogen in the urine of a period was recorded in each experiment at the end of the first hemorrhage period. In nearly all the hemorrhage periods the average daily amount of nitrogen, in the urine of the three days that opened a period after hemorrhage, was higher than the average for the three days that closed the preceding period.

In the first experiment the average daily elimination of nitrogen in the urine was greater after all but two of the hemorrhages than during the normal period. In the same experiment the nitrogen

of the fæces exceeded the normal fæcal elimination after only two of the five hemorrhages. In the second experiment the average daily excretion of urinary nitrogen after *each* hemorrhage was equal to or greater than that of the normal period. The same was true of the fæces, except for the last period.

During the early stages of such experiments as these, when the ordinary blood surplus is not too greatly reduced, it is probable that appreciable proportions of the absorbed nitrogenous and other matters from the transported blood are not utilized but quickly excreted, as when an excess of protein food is taken. Later, in experiments of this kind, after thorough depletion of the circulating blood surplus, the absorbed matters from the transposed blood, whether changed or not, are probably more completely utilized and retained after their return to the circulation.

Sulphur catabolism. — In the first experiment there was, in each period, a retention of sulphur — all the period average daily balances were small “plus balances” in fairly close agreement. In the second experiment the balances were “plus balances” except after two of the seven hemorrhages. Retention of sulphur in the second experiment was greatest in the normal period.

In the first experiment the period average daily sulphur difference was smaller than that of the normal period after three hemorrhages, and larger than the normal balance after two hemorrhages. In the second experiment all the sulphur “plus balances” were much less after the hemorrhages than after the first period of normal conditions. In a very general way the total excretion of sulphur, as in the case of nitrogen, was slightly increased after internal hemorrhage. This result is in accord with the effect of external hemorrhage on sulphur catabolism. In both normal periods and in seven of the eleven hemorrhage periods the signs of the sulphur and nitrogen balances were the same (see Tables XI and XXII).

The urinary and fæcal eliminations of sulphur were, in terms of daily averages, only slightly affected by the hemorrhages in most instances.

Phosphorus catabolism. — In the first experiment there was retention of phosphorus in the normal period and in three of the five hemorrhage periods. In each of these three hemorrhage periods the amount of retained phosphorus was greater than that in the normal period. In the second experiment there was again retention of

phosphorus in the normal period, but in only one of the six hemorrhage periods. The phosphorus results for the two experiments were therefore not in accord. In a very general way, however, phosphorus excretion was somewhat increased after hemorrhage, in harmony with the results for nitrogen and sulphur. In their study of the effects of external hemorrhage Hawk and Gies found that there was "a variable effect on the elimination of phosphorized substances, though mainly a decreased excretion of the latter."

The daily average urinary and faecal eliminations of phosphorus were not as uniform as those of sulphur after the hemorrhages. The large quantity of phosphate in the bone ash of the diet, with the increased difficulties of accurate analysis, may have had some influence in this connection.

In both normal periods and in six of the eleven hemorrhage periods the signs of the phosphorus and nitrogen balances were the same. In both normal periods and in six of the eleven hemorrhage periods the signs of the phosphorus and sulphur balances were identical. In both normal periods and in four of the eleven hemorrhage periods the signs of the nitrogen, sulphur, and phosphorus balances were in agreement (see Tables XI and XXII).

General observations. — The mammalian organism probably has a fairly large reserve supply of blood. *External* loss of a moderate amount of this surplus from a healthy animal seems to have little or no harmful effect. Hurtful influences of hemorrhage are less apt to be exerted, all other conditions being equal, if the blood passes from the vascular system to the peritoneal cavity, instead of away from the body. It is only when the vascular drain is comparatively great, in cases of internal hemorrhage, or under ordinary conditions of excessive external hemorrhage, that decisive modification of general metabolic factors is effected. Hemorrhage in any degree naturally results in metabolic disturbances, slight though they may be.

Neither sugar nor protein, in abnormal quantities, could be detected in any of the urines of these experiments.

We could not carry our experiments far enough to obtain answers to the open questions connected with the ultimate causes of some of the more important excretory phenomena we have observed, but it is Dr. Gies's intention to continue his study of this subject with more intimate inquiries into these and related matters. For this reason we refrain from indulging the temptation to offer additional hypotheses in explanation of the metabolic data herein recorded.

VI. PRACTICAL APPLICATION.

It would seem that with an organism in healthy condition a hemorrhage which did not endanger life, *e. g.*, 1 per cent to 2 per cent of body weight, would do little or no harm, especially if intraperitoneal. Repeated losses of blood would cause increasing damage, but relatively less if intra-abdominal instead of external. It is only after great cumulative losses or after an overwhelming single hemorrhage that the system does not recover promptly, if at all. In the case, then, of such losses of blood as occur from a ruptured ectopic pregnancy or ruptured spleen or liver, with the hemorrhage stopping without surgical interference, the blood, *per se*, may be not only devoid of harm, but of special use in the body. Such use would be influenced, however, by possible infections and adhesions. If surgical intervention were contemplated in such cases, the surgeon would have to consider these possibilities and the probable effects. With the patient placed so that the blood would gravitate toward the diaphragm, *i. e.*, with feet raised, the blood would collect where absorption would be very rapid, where infection could best be met, and where, if adhesions should form, they would do a minimum of harm, *i. e.*, between the suphrenic organs and away from the intestines and pelvic viscera. The more rapid the absorption, the less the likelihood of adhesions. We fully appreciate the fact, however, that observations of this kind pertaining primarily to the dog cannot be applied automatically to man. Very thorough and very discriminating study of human cases must be conducted before such conclusions can be accepted for practical guidance.

VII. SUMMARY OF GENERAL CONCLUSIONS.

After internal hemorrhage equal to from 2.85 to 5.56 per cent of the body weight of dogs, the weight of the animals declined perceptibly. The maximal volume of urine was usually excreted on the second day after internal hemorrhage. The specific gravity of the urine was increased on the days of internal hemorrhage. There were no constant effects, if any, on the reaction of the urine.

There were no marked influences of internal hemorrhage on the weight or consistency of the fæces nor on the fæcal eliminations of nitrogen, sulphur, and phosphorus. No particular influence was

exercised on digestion or assimilation. There was no appreciable effect on the secretion into the alimentary tract of nitrogenous matter, such as mucus.

Either ether anæsthesia or internal hemorrhage, or both, were devoid of pronounced disturbing influences as measured by us, on the general metabolism of the dogs in these experiments, or their effects were mutually antagonistic in the main and, therefore, not discernible for more than a day or two, if at all. In a very general way the total excretions of nitrogen, sulphur, and phosphorus were slightly increased after the internal hemorrhages.

Neither sugar nor protein, in abnormal quantities, could be detected in any of the urines of these experiments.

Comparative observations are summarized on p. 238.

We gladly embrace this opportunity to thank Professor William J. Gies for constant supervision of the work, which he suggested and guided. We also wish to acknowledge our indebtedness to Drs. Welker and Berg and Mr. Seifert for much helpful assistance.

BIOGRAPHICAL

Frederick Seymour Weingarten received his preliminary education in the New York public schools, the College of the City of New York, and the South Division High School, Chicago. He matriculated at the University of Chicago in 1892. In 1894 failing eyesight interrupted his studies, and he entered the commercial field in New York. From 1892 to 1896, he taught in public schools in New York or Chicago. In 1902, he matriculated at the College of Physicians and Surgeons, and graduated in 1907, an attack of septico-pyemia delaying him a year. In the summer of 1904, he returned to Chicago University and there received the B. S. degree. In the fall of 1904, he began special work at Columbia University, leading to the degree of Ph. D. During the summer of 1907, he carried out a series of observations on tuberculous cases at the Stony Wold Sanatorium and then entered the J. Hood Wright Hospital, where he now serves.

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